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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/755,398	01/04/2001	Joel S. Bader	15966-632 (CURA-132)	5250

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EXAMINER	
HASHEMI, SHAR S	

ART UNIT	PAPER NUMBER
1637	9

DATE MAILED: 06/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/755,398	BADER ET AL.
	Examiner	Art Unit
	Shar Hashemi	1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/26/02*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 January 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Drawings

1. The titles of drawings are objected to because the titles in Figures 3 & 6 contain words that are misspelled. In the title of Figure 3, **primeres** must be changed to *primers*. In the title of Figure 6, **idnetification** must be changed to *identification*. A proposed title of drawing correction or corrected titles are required in reply to the Office action to avoid abandonment of the application. The objection to the title of the drawings will not be held in abeyance.

Applicant is required to submit a proposed description of drawing correction in reply to this Office action. However, formal correction of the noted defect may be deferred until after the examiner has considered the proposed title of drawing correction. Failure to timely submit the proposed title of drawing correction will result in the abandonment of the application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-10 are indefinite because in claim 1 it is unclear whether the method for identifying, classifying, or quantifying nucleic acids includes or does not include a sequencing step.

B) Claims 11-15 are indefinite because in claim 11 it is unclear whether the method for extending the sequence in a length-subsequence combination of nucleic acids includes or does not include a sequencing step.

C) The phrase "additionally includes" and term "sequencing" renders claim 7 indefinite. It is unclear whether "additionally includes" refers to performing this sequencing step before or after the nucleotide database search step. It is also unclear as to whether "sequencing" refers to traditional sequencing using the Sanger method or non-traditional sequencing using the Rothberg method.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1 & 6-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Rothberg et al (WO 97/15690 May 1, 1997).

Claims 1 & 6-10 are drawn to a method for identifying, classifying, or quantifying nucleic acids with different nucleotide sequences in a sample, comprise probing a sample with a recognition means, generating a first signal that represents the length and the identity of the target subsequences in the targeted nucleic acid, selecting a targeted nucleic acid, extending the sequence information under conditions that generate a second signal, and searching a nucleotide sequence database to determine the presence of a match under conditions that the sequence

which generated a second signal shares the same length and same target subsequence with the database sequence. Claim 11 is drawn to a method for extending the sequence in a length-subsequence combination, comprise probing a sample with a recognition means, generating a first signal that represents the length and the identity of the target subsequences, selecting targeted nucleic acids, extending sequence information that generates a second signal from a subsequence which has been extended.

Rothberg et al in WO 97/15690 teach a method for identifying, classifying, or quantifying nucleic acids in a sample without sequencing by utilizing restriction endonucleases (see whole document especially page 8, lines 17-37). They teach probing the sample with a recognition means (page 14, lines 25-29). They teach generating signals arising from a nucleic acid in the sample representing the length and the identities of the target subsequences (page 14, lines 29-37). They teach choosing targeted nucleic acids (page 15, lines 1-13). They teach extending the target sequences with a DNA polymerase in order to generate another signal that has the same length and the same identity as the target subsequence (page 16, lines 19-37). They teach determining a match between the generated signal and known nucleotide sequences from a nucleotide sequence database comprised of sequences that have the same length and the same target subsequence as the generated signal (page 15, lines 1-14). They teach a sequence from the database that matches the generated signal in length and target subsequence (page 15, lines 14-28). They teach recovering a nucleic acid fragment and obtaining its sequence (page 17, lines 17-27). They teach the plurality of nucleic acids are DNA (page 16, lines 5-8). They also teach a probing step that comprises of digesting with a restriction endonuclease that produce overhangs, hybridizing double-stranded adapter DNA molecules to the overhang produced by the

restriction endonuclease, and ligating the adapter DNA molecules to the fragments to produce ligated fragments (page 16, lines 17-34). They teach the plurality of nucleic acids are RNA (page 16, lines 10-12). They teach a method of extending the sequence in a sample by utilizing restriction endonucleases (see whole document especially page 16, lines 17-37). They teach probing the sample with a recognition means (page 14, lines 25-29). They teach generating signals arising from a nucleic acid in the sample representing the length and the identities of the target subsequences (page 14, lines 29-37). They teach choosing targeted nucleic acids (page 15, lines 1-13). They teach extending the target sequences with a DNA polymerase in order to generate another signal that has the same length and the same identity as the target subsequence (page 16, lines 19-37).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 2-5, & 12-15 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Rothberg et al (WO 97/15690 May 1, 1997) in view of Rothberg et al (WO 99/07896 February 18, 1999).

Claims 1 & 11 were previously discussed. Claims 2 & 3 which are drawn to claim 1 with the further limitation of an oligo-competition signal. Claim 4 which is drawn to claim 1 with the further limitation of labeled primers and an unlabeled primer. Claim 5 which is drawn to claim 1

Claims 1 & 11 were previously discussed. Claims 2 & 3 which are drawn to claim 1 with the further limitation of an oligo-competition signal. Claim 4 which is drawn to claim 1 with the further limitation of labeled primers and an unlabeled primer. Claim 5 which is drawn to claim 1 with the further limitation of labeled primers having subsequences of an unlabeled primer. Claims 12 & 13 which are drawn to claim 11 with the further limitation of an oligo-competition signal. Claim 14 which is drawn to claim 11 with the further limitation of labeled primers and an unlabeled primer. Claim 15 which is drawn to claim 11 with the further limitation of extending sequence information by contacting a nucleic acid sample with labeled and unlabeled primers.

Rothberg et al in WO 97/15690 teach a method for identifying, classifying, or quantifying nucleic acids in a sample without sequencing by utilizing restriction endonucleases (see whole document especially page 8, lines 17-37). They teach probing the sample with a recognition means (page 14, lines 25-29). They teach generating signals arising from a nucleic acid in the sample representing the length and the identities of the target subsequences (page 14, lines 29-37). They teach choosing targeted nucleic acids (page 15, lines 1-13). They teach extending the target sequences with a DNA polymerase in order to generate another signal that has the same length and the same identity as the target subsequence (page 16, lines 19-37). They teach determining a match between the generated signal and known nucleotide sequences from a nucleotide sequence database comprised of sequences that have the same length and the same target subsequence as the generated signal (page 15, lines 1-14). They teach labeled primers (page 38, lines 14-18). They teach a sequence from the database that matches the generated signal in length and target subsequence (page 15, lines 14-28). They teach recovering a fragment of a nucleic acid in the sample (page 17, lines 16-27). They teach the plurality of nucleic acids

are DNA (page 16, lines 5-8). They teach a probing step that comprises of digesting with a restriction endonuclease that produce overhangs, hybridizing double-stranded adapter DNA molecules to the overhang produced by the restriction endonuclease, and ligating the adapter DNA molecules to the fragments to produce ligated fragments (page 16, lines 17-34). They teach the plurality of nucleic acids are RNA (page 16, lines 10-12). They teach a method of extending the sequence in a sample by utilizing restriction endonucleases (see whole document especially page 16, lines 17-37). They teach probing the sample with a recognition means (page 14, lines 25-29). They teach generating signals arising from a nucleic acid in the sample representing the length and the identities of the target subsequences (page 14, lines 29-37). They teach choosing targeted nucleic acids (page 15, lines 1-13). They teach extending the target sequences with a DNA polymerase in order to generate another signal that has the same length and the same identity as the target subsequence (page 16, lines 19-37).

Rothberg et al in WO 97/15690 do not teach negative or positive oligo-competition signals. They do not teach an unlabeled primer.

Rothberg et al in WO 99/07896 teach an oligo-poisoning signal (see whole document especially page 27, lines 1-32). They teach unlabeled "poisoning" primer (page 22, lines 10-24). They teach an advantage of "poisoning" primer is to provide increased discrimination and resolution (page 7, lines 26-27).

One of ordinary skill at the time the invention was made would have been motivated to apply Rothberg et al's WO 99/07896 method of oligo-poisoning to Rothberg et al's WO 97/15690 method of determining and classifying sequences in order to perform a highly specific quantitative determination of the components of a cDNA mixture prepared from a tissue sample

in a rapid, economical and reproducible manner (page 6, lines 1-20). It would have been prima facie obvious to apply Rothberg et al's WO 99/07896 method of oligo-poisoning to Rothberg et al's WO 97/15690 method of determining and classifying sequences in order to accurately and efficiently confirm a putatively identified sequence of a nucleic acid fragment in a sample of nucleic acids.

SUMMARY

5. No claims are allowed.

CONCLUSION

6. Any inquiry concerning this communication or earlier communication should be directed to Shar Hashemi whose telephone number is (703) 305-4840 and whose e-mail address is Shar.Hashemi@uspto.gov. However, the Office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner is on flex-time schedule and can best be reached on weekdays from 7:00 a.m. to 3:30 p.m. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist for Technology Center 1600 whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official

Gazette, 1096 OG 30 (November 15, 1989). The CM1 Center numbers for Group 1600 are Voice (703) 308-1235 and Before Final FAX (703) 872-9306 or After Final FAX (703) 308-9307.

June 13, 2002

JEFFREY SIEW
PRIMARY EXAMINER
6/17/02